Comparison of Crossed-spinal modulation of the H-reflex between sedentary older adults and high-risk fallers

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Abstract

The purpose of this study was to compare crossed-spinal H-reflex modulation between healthy older adult subjects and older adults who are at a high risk of falling. 18 subjects participated in this study, and were divided into two different groups: 1) 14 neurologically healthy adults over the age of 65 (Age = 75.2 yrs; SD = 6.26); 2) 4 older adults determined by physicians or physical therapists to be high-risk fallers (Age = 78.3 yrs; SD = 4.02). Fall risk was based on history of previous falls and/or Tinetti balance scores. The variable being measured in this study was a spinal stretch reflex known as Hofmann reflex, or H-reflex. Subjects were asked to lie in the prone position for testing. In order to record muscle activity, EMG electrodes were placed on the left tibialis anterior and the right soleus muscles. Stimulating electrodes were then placed over the common peroneal nerve (CPN) of the left leg and the tibial nerve of the right leg. Baseline measurements were recorded for maximal motor response (M-max), maximal H-reflex response (H-max), and tibialis anterior motor threshold. For control measurements, a single stimulation was delivered to the right tibial nerve to evoke a motor response in the soleus. The intensity used for controls was set to 50% of H-max. For the conditioning protocol, stimulation was first delivered to the CPN at 1.2x motor threshold, then a tibial nerve stimulation

followed at varying intervals of 25ms, 50ms, 75ms, 150ms, or 300ms. The goal of this conditioning protocol was to determine the effect that antagonist muscle activation has on its contralateral agonist’s spinal reflexes. Results showed a significant interaction between healthy older adults and high-risk fallers ($F_{5,45} = 4.21$, $p < 0.05$), specifically at the 75ms, 150ms, and 300ms intervals. While the healthy adults were able to modulate spinal reflexes based on the time interval, the high-risk fallers showed no modulation across intervals. This inability to properly modulate spinal reflexes could help to explain why these individuals fall more frequently.

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Chapter 1
Introduction

Spinal cord plasticity plays a significant role in tasks such as balance and postural control during ambulation. One way to measure this plasticity is through the Hoffmann reflex, or H-reflex (Trimble & Koceja, 1994). Since reflex pathways are not exclusively dependent on cortical input, they are able to respond more quickly to obstacles in the environment that may perturb one's balance. In normal, healthy individuals, modulation of these reflexes takes place during complex visuo-motor tasks (Perez, Lungholt, & Nielsen, 2005), and even during more basic tasks such as balance training (Trimble & Koceja, 2001). Reflex pathways also modulate based on position of the subjects, whether they are standing or seated (Koceja, Trimble, & Earles, 1993). The more unstable the position or surface is, the more the H-reflex is down-regulated.

Any deficit in an individual's ability to modulate the H-reflex can result in balance and postural detriments. The aging process is accompanied by a variety of different cognitive and motor impairments (Dinse, 2006; Krampe, 2002; Persson et al., 2006). Some of these impairments include decreased amplitude of reflex waves and the inability to modulate the H-reflex (D. M. Koceja & Mynark, 2000; Morita, et al., 1995; R. G. Mynark, 2005). Unlike young subjects, older adult subjects do not demonstrate decreased amplitude of H-reflex activity when moving from a prone position to standing (D. M. Koceja, et al., 1995). These deficits in the ability to modulate have also been expressed during walking (Chalmers & Knutzen, 2000). The inability to effectively modulate reflex pathways can lead to motor deficits and an increased risk of falling. As a result, this population becomes less physically active and their quality of life diminishes.

Another important factor in maintaining balance and posture is the crossed-spinal communication, or how well the body coordinates movement between an extremity and its contralateral counterpart. This was first discovered by Sherrington, who noticed that a stimulus that produces a flexion reflex will also cause movement in the contralateral limb (C. S. Sherrington, 1910a). One application of this mechanism in everyday activity would be stepping on a sharp object. Since the ipsilateral limb responds by withdrawing quickly from the painful stimulus, the contralateral limb must also respond by facilitating the extensor muscles and inhibiting the flexor muscles. In laboratory research, this crossed-spinal pathway has also been determined to be associated with obstacle avoidance (Stubbs & Mrachacz-Kersting, 2009). This is particularly important during ambulation on any unstable surface or any surface that is not smooth and unobstructed.

Much like the spinal H-reflex, electromyography patterns have shown a detriment in crossed-spinal reflexes among the older adult population (Kamen & Koceja, 1989). For young, healthy subjects, tendon tap reflexes of the patellar tendon revealed an inhibition in the contralateral limb at short-latency intervals (0-50ms), and facilitation at longer-latency intervals (60-200ms). The peak facilitation was also delayed by about 75ms in the older adults, which suggests that they may also have slower nerve conduction velocity (figure 1). This increase in inhibition and excitation can cause deficits in bilateral coordination, which results in insufficient recovery from a rapid perturbation during a fall.

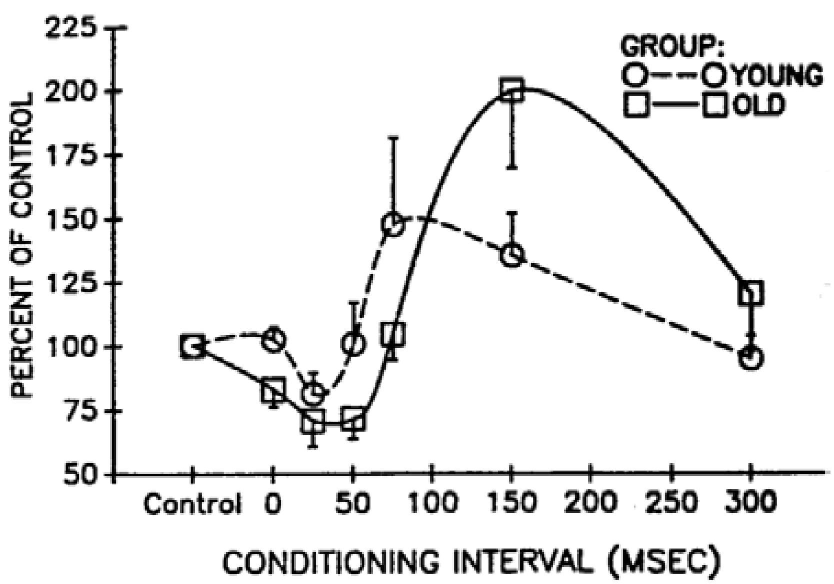

Figure 1.Asymmetry in crossed-spinal reflexes in older adults.

Peak reflex force following a conditioning tendon tap in the contralateral limb. Reflex force is represented as a percentage of the control reflex. Older adult subjects show larger deviations from 100% compared to the young. Also, there is a shift in peak facilitation in the old group from approximately 75ms in young subjects to 150ms in old subjects. From Kamen and Koceja (1989).

Although the aging process naturally degenerates neural pathways and decreases their ability to function effectively, research suggests that these effects may be minimized via physical activity. In a young, healthy population of subjects, participants displayed an increase in peak-to-peak H-reflex amplitude from baseline values following an exercise program that required two hours of running per week (Pérot, Goubel, & Mora, 1991). In the older adult population, motor skill training has provided evidence that older adults also have some ability to modulate spinal reflexes to effectively recover from perturbation (Mynark & Koceja, 2002). However, another study revealed that 16 weeks of strength training for the plantar flexors did not yield any changes in spinal reflexes, despite improvements in strength (Scaglioni, et al., 2002). This suggests that spinal reflexes may not be as flexible in older adults as they are in younger subjects, but do still have adaptive potential. Since spinal circuits demonstrate plasticity following exercise training, and older adult subjects do appear to have potential for modulation and plasticity in the spinal cord, the role of exercise in preserving the spinal circuitry is essential to explore. The purpose of this study was to examine crossed-spinal communication in the reflex pathways between a groups of identified high-risk fallers and a groups of age-matched sedentary subjects.

Chapter 2

Review of Literature

Hoffmann Reflex

The Hoffmann Reflex (H-reflex) has been used extensively in research to measure spinal excitability. It is the electrical equivalent of the tendon-tap paradigm used to elicit a spinal stretch reflex. Since the H-reflex is monosynaptic, meaning the afferent nerve synapses directly with an alpha motoneuron, it can provide an accurate measurement of spinal excitability, so long as the experiment is well-controlled (Zehr, 2002). Evoking an H-reflex is accomplished by electrically stimulating a mixed nerve, which means that it contains both sensory afferent and motor efferent nerves (Zehr, 2002). This electrical volley can be visualized in Figure 2. The stimulus, represented by the smaller gray ellipse in image 2A, evokes an initial motor response from the stimulation site to the muscle, which is known as the M-

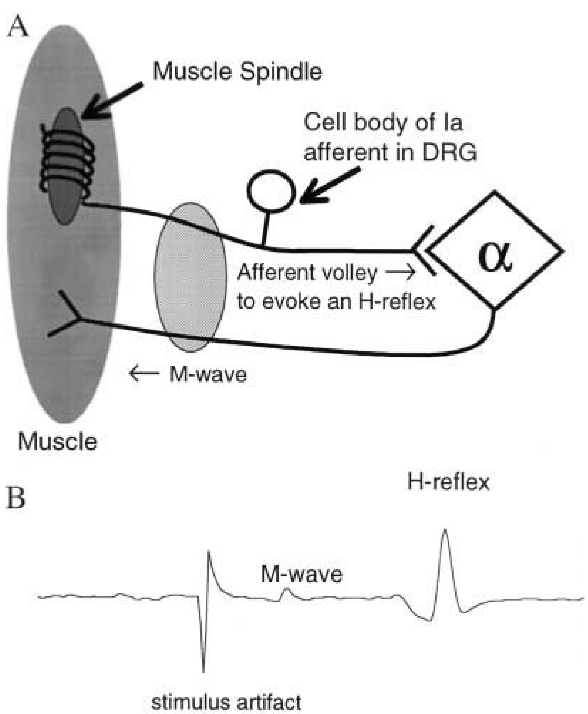

Figure 2: From Zehr, 2002

1A: Schematic showing how a stimulus (small gray ellipse) evokes an M-wave and H-reflex

1B: EMG trace shows the time and amplitude difference between M-wave and H-reflex following a stimulus wave. It also induces a response in the afferent nerve, which synapses with the alpha motoneuron to produce a second muscle response. This second response is the H-reflex (Zehr, 2002).

Modulation of H-Reflex

The H-reflex is modulated differently throughout several different motor tasks (Perez, Lungholt, & Nielsen, 2005). Perhaps the most simplistic of these tasks is postural position. Koceja et al. observed that when a person moves from a prone position to a standing position, the H-reflex is depressed (Koceja et al., 1993). Depression of the H-reflex is also seen when standing without any support, as compared to standing with back support (Katz, Meunier, & Pierrot-Deseilligny, 1988). These data give credence to the notion that as the stability of an individual's posture decreases, the H-reflex also diminishes (Koceja et al., 1993).

Modulation of the H-reflex is not exclusive to simple motor tasks, but rather extends to more complex motor skills. Similarly to the relationship between postural stability and H-reflex modulation, Capaday and Stein found increased inhibition during an escalation in task complexity. Their research showed that the H-reflex is down-regulated during walking, as compared to standing (Capaday & Stein, 1986). This finding is further supported by the work of Perez et al., whose research revealed a depression of the H-reflex after a complex visuo-motor task.

Subjects in this study were shown images of specific ankle motions on a computer screen, and were then asked to mimic these motions. Immediately following the training sessions, EMG recordings of H-reflex showed a depression of about 20% from baseline (Perez et al., 2005). Modulation of the soleus H-reflex is of particular interest, as the goal of this study is to determine whether or not high risk fallers modulate differently from otherwise healthy older adults.

Presynaptic Inhibition

As previously mentioned, the H-reflex can provide a measurement of alpha motoneuron excitability, but only under well-controlled circumstances. There are confounding factors that must be considered, as they can significantly affect reflex responses. The main factor to take into account is presynaptic inhibition (Zehr, 2002). Presynaptic inhibition (PI) is a result of descending tonic influence, and is mediated by supraspinal structures (Pierrot-Deseilligny & Burke, 2005). A key role of presynaptic inhibition is to control the amount of sensory information that passes from Ia afferents onto alpha motoneurons when planning or executing movement (Rudomin, 2009). This control of flow is accomplished via first-order primary afferent depolarization interneurons (PAD), which are inhibitory interneurons that synapse with motor neurons (Pierrot-Deseilligny & Burke, 2005).

Presynaptic inhibition can be measured using a several different techniques. One method is to stimulate the antagonist muscle’s motor nerve a short time before stimulation of the agonist. A commonly accepted interstimulus interval is between 80 and 100 ms (Knikou, 2008). For instance, to measure the amount of PI on a person’s soleus (SOL) H-reflex, one could first stimulate the common peroneal nerve (CPN) to evoke a response in the tibialis anterior (TA) 80-100ms before stimulating the soleus. Since the TA has reciprocal neural connections to the soleus, stimulation of CPN will activate first-order PAD INs of the soleus, which results in presynaptic inhibition (Pierrot-Deseilligny & Burke, 2005).

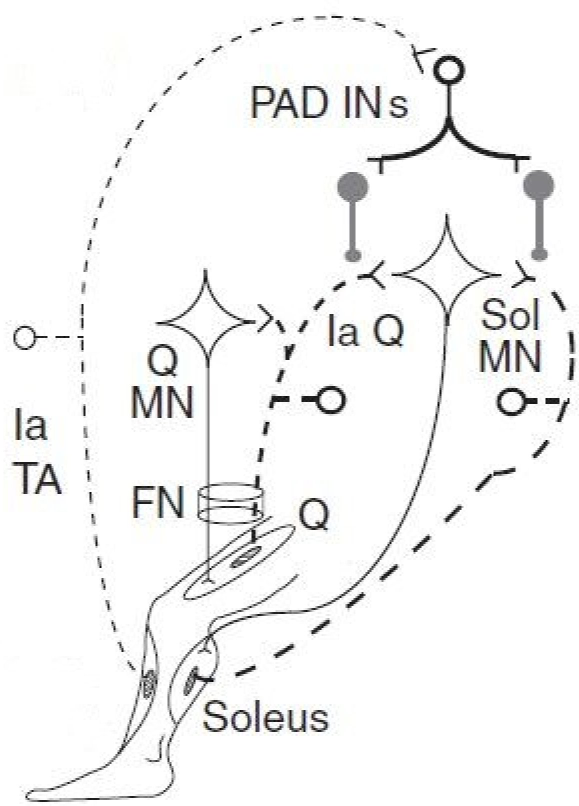

Figure 3: (Pierrot-Deseilligny & Burke, 2005). Schematic shows the neural connections between the muscles of the lower limb and describes how stimulation of one muscle group can affect the output of others.

Presynaptic inhibition can also be measured indirectly through heteronymous facilitation (Hultborn, Meunier, Pierrot-Deseilligny, & Shindo, 1987). Heteronymous facilitation is a result of the synergism that exists between the quadriceps and soleus muscles. While muscle spindles in the quadriceps project to homonymous motor neurons of the quadriceps, they also project to heteronymous motor neurons of the soleus (Pierrot-Deseilligny & Burke, 2005). Measuring presynaptic inhibition with this method requires that the stimulation of soleus afferents precede stimulation of the femoral nerve of the quadriceps. The reason for this is the proximity of the femoral nerve to the spinal cord, relative to the soleus. This negative conditioning results in facilitation of the soleus H-reflex, which can be an indirect measurement of PI such that larger H-reflex amplitudes after conditioning represent less presynaptic inhibition (Hultborn et al., 1987).

Aging

The aging process can have a significant influence on the H-reflex and its modulation. At the cortical level, aging causes a substantial amount of reorganization of brain structures, which results in functional differences (Dinse, 2006). However, these differences do not necessarily mean that deficits will arise. Lee et al found that although older rats utilized different mechanisms than young rats to generate long term depression, they were still capable of doing so (Lee, Min, Gallagher, & Kirkwood, 2005).

Summary

From the literature presented, the H-reflex provides a reliable and valid measurement of spinal cord reflex pathways. This measurement can be used to infer both facilitation and inhibition acting at the level of the motoneurons. It is also apparent from the literature that these reflex pathways are modulated given different environmental demands. Most likely, presynaptic networks are responsible for maintaining this modulatory capacity. Finally, aging produces a variety of changes in the reflex networks, including an inability to properly modulate these circuits in response to changing environmental demands.

Chapter 3

Methodology

Subjects

A total of 18 subjects were recruited for this study. The subjects were divided into two different groups. The first group consisted of 14 older adult subjects over the age of 65. The second group was 4 older adults who were considered 'high risk fallers.' These subjects were referred to the lab by their physicians or physical therapists if they determined that the subjects had a history of falling and were at a high risk of falling again in the future. In addition to the aforementioned criteria, all subjects were able to stand independently or with an assistive device such as a cane for at least five minutes, and walk for five minutes independently or with an assistive device such as a cane or a walker. Subjects were excluded from the study if they met any of the following criteria:

1) Body mass index > 31kgm^{-2}
2) Uncontrolled hypertension (resting systolic > 170 mmHg, diastolic > 100 mmHG)
3) Symptomatic coronary artery disease
4) Prior or current neurological or neuromuscular disorder
5) Myocardial infarction in the last 12 months
6) Peripheral neuropathy (diabetic and idiopathic)
7) Stroke
8) Intermittent claudication with symptoms at < 150 m of walking

9) Dizziness
10) Vertigo
11) Cancer –chemotherapy within 6 months
12) Pulmonary embolism or thrombophlebitis within 6 months
13) Pulmonary disease requiring chronic O_2.
14) Unable to find a recordable and measurable soleus H-reflex and motor responses from the tibialis anterior

All subjects signed an informed consent form, and were asked to fill out a general health questionnaire to evaluate their health history and current state of health.

Equipment

To record reflex activity of the lower limb, active bipolar electrodes were placed on the soleus and tibialis anterior muscle of both legs. The signals from recording electrodes were amplified with a gain of 1000x (Delsys Bagnoli 16-EMG system). For digitization, WinDaq Pro Data Acq™ system was used to record EMG signals and output from stimulators with sampling rate set at 2000 Hz. Two types of stimulators were used for this study; GRASS, S88 model (Astro-Med Inc.) and model DS7A from DIGITIMER Limited. A stimulus isolation unit (GRASS, SIU5) and a constant current unit (GRASS, CCU) were connected with the GRASS stimulator to ensure subjects' safety. A custom Matlab® (MathWorks, Inc.) program was used to calculate the variables from sampled signals of EMG for analysis.

Experimental Procedures

Both stimulating and recording electrodes were placed on the lower limbs bilaterally to record data from the soleus (SOL) and tibialis anterior (TA) muscles. Bipolar surface electrodes were used to record EMG activity of the muscles. For the SOL, the electrode was placed on the inferior, posterior lower leg, parallel with the muscle fibers and just superior to the Achilles tendon. The TA electrode was positioned lateral to the medial shaft of the tibia, approximately one-third the distance between the knee and the ankle, and parallel with the muscle fibers. Two sets of stimulating electrodes were used to stimulate the posterior tibial nerve of the right leg and the common peroneal nerve of the left leg (Figure 4). For stimulation of the right tibial nerve, an 8mm diameter cathode electrode was placed in the popliteal fossa and a 4 cm diameter anode electrode was placed just superior to the patella. For left common peroneal nerve stimulation, a bipolar electrode with an 8 mm diameter and a 1 cm interelectrode distance was placed just distal to the fibular head. The 4 cm diameter anode electrode was placed over the lateral malleolus.

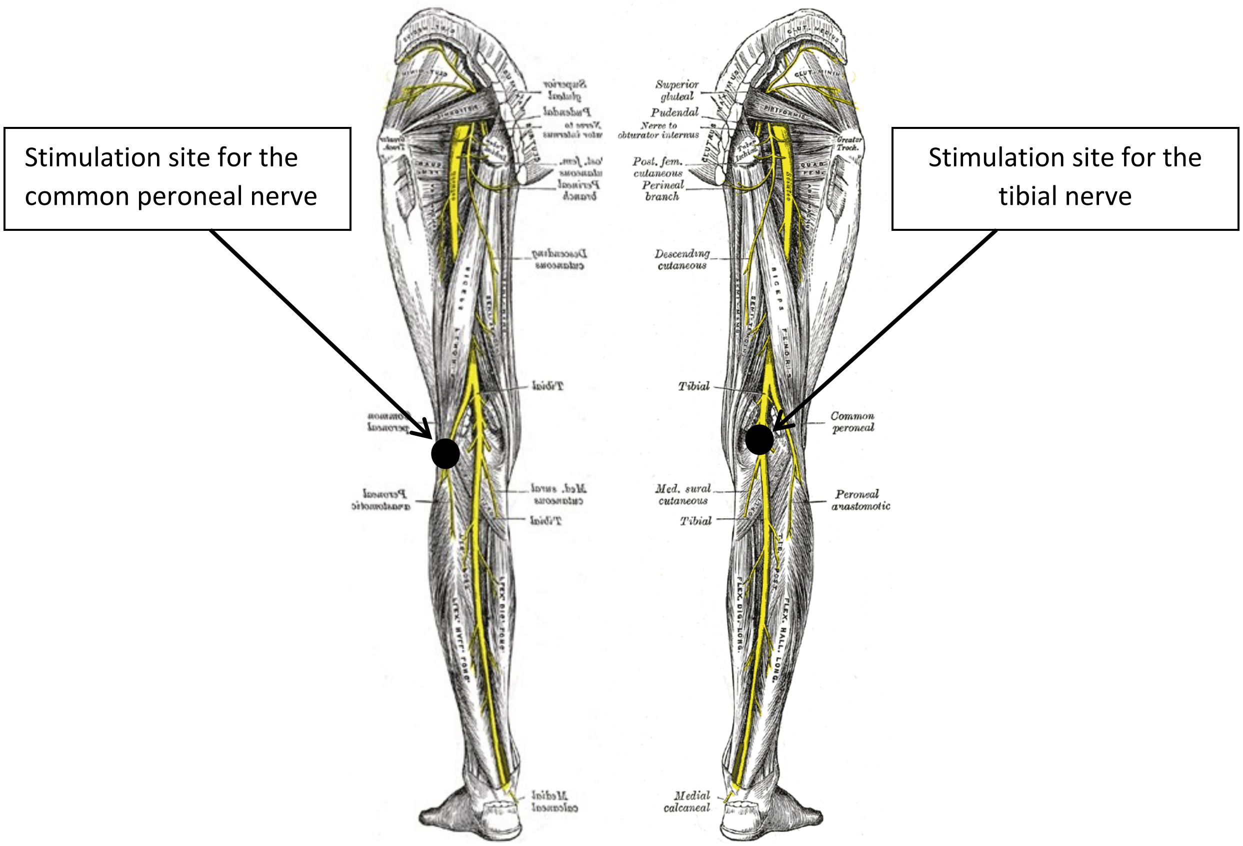

Figure 4. Stimulation sites for crossed-spinal reflex conditioning: Depicting the location of both the tibial nerve and the common peroneal nerve. The black dots represent stimulation sites. The left leg received common peroneal nerve stimulation and the right leg received tibial nerve stimulation.

Experimental Protocol

Following the electrode placement, subjects were asked to lie in the prone position for the duration of the experimental testing. Before the condition protocol took place, each subject was tested to find a maximal motor response (M-max), maximal H-reflex response (H-max), and 50% of the H-max in the right leg, which was used as the control H-reflex intensity. A 1 ms square wave pulse was used to stimulate the posterior tibial nerve of the right leg and evoke the H-reflex. To stimulate the common peroneal nerve of the left leg, a 1ms pulse was used to evoke a motor response. Stimulation intensity for the common peroneal nerve was set to 1.2x motor threshold. A series of 15 control H-reflexes were tested at 50% of the H-max prior to conditioning. To assess crossed-spinal reflex modulation, a conditioning stimulus was delivered to the common peroneal nerve of the left leg using a 160 Hz train, 20 ms in duration, at 1.2x motor threshold. This was followed by stimulation of the posterior tibial nerve of the right leg, which produced an H-reflex. An interval of 10 seconds was used between each trial to reduce any potential recurrent inhibition. This study used a series of conditioning intervals to assess the time-course modulation of contralateral conditioning on the soleus H-reflex. The following conditioning intervals between the left leg conditioning stimulus and the right leg soleus H-reflex were used: 0ms, 25ms, 50ms, 75ms, 150ms and 300ms. The conditioning protocol is illustrated in figure 5. Each conditioning interval was tested 10 times, resulting in 60 conditioned H-reflex responses. These conditioning intervals were chosen based on prior research done by Koceja and Kamen (1992), which demonstrated that the amount of inhibition or excitation in the test reflex is dependent on the conditioning-test interval, and that modulation in the reflex can been seen across a wide range of conditioning intervals. Total experimental time for each subject was approximately 1 hour and 30 minutes. A custom Matlab® (MathWorks, Inc.) was used to randomly assign subjects to a conditioning interval order.

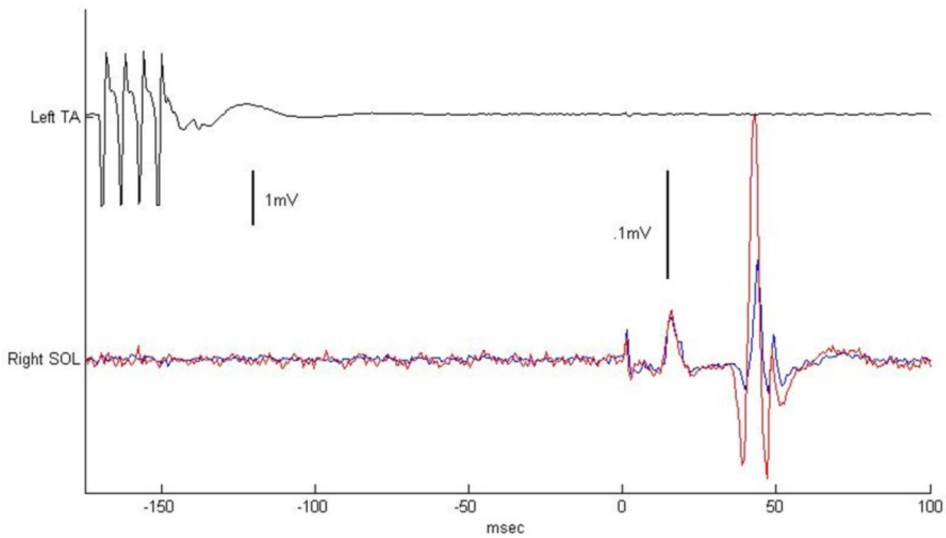

Figure 5. Contralateral conditioning of the soleus H-reflex: The EMG trace depicts the conditioning contralateral stimulation to the CPN, which occurred 150 ms prior to the test ipsilateral soleus H-reflex. Although this figure only depicts a 150 ms conditioning-test interval, 25 ms, 50 ms, 75 ms, and 300 ms intervals were also tested.

Chapter 4

Results

The purpose of this study was to compare crossed-spinal H-reflex modulation between healthy older adult subjects and older adults who are at a high risk of falling. This chapter will present the results of the study. This chapter will be divided into the following sections: 1) description of subjects; 2) crossed-spinal results.

Description of Subjects: A total of 18 subjects participated in this study. Subjects were divided into two different groups: 1) 14 neurologically healthy adults over the age of 65 (Age = 75.2 yrs; SD = 6.26); 2) 4 older adults determined by physicians to be high-risk fallers (Age = 78.3 yrs; SD = 4.02). All subjects met the inclusion criteria described in the methodology section. Subject demographics are outlined in Table 1.

Table 1: Comparison of age (in years) between the two experimental groups

Group	*Minimum*	*Maximum*	*Mean*	*Standard Deviation*
Older Adults	67	87	75.2	6.26
High-Risk Fallers	72	83	78.3	4.02

Crossed spinal reflexes. Due to the differences in unilateral reflexes between the groups, older adults were tested at a control H-reflex of 25% of M-max, whereas the high-risk fallers were tested at a control h-reflex of 17% of M-max. Ideally, the testing conditions would remain consistent between all subjects involved. However, this was methodologically not possible for the high-risk group. In terms of crossed-spinal reflexes, a significant interaction was observed between the older adult subjects and the high-risk fallers ($F_{5,45} = 4.21$, $p < 0.05$), as displayed in Figure 6. This difference was more pronounced at the longer-latency intervals (50 ms, 75 ms, and 150 ms). For example, the older adults produced 34% facilitation at 50 ms, 33% at 75 ms, and 39% at 150 ms, while the high-risk fallers maintained about 13% of M-max across all intervals.

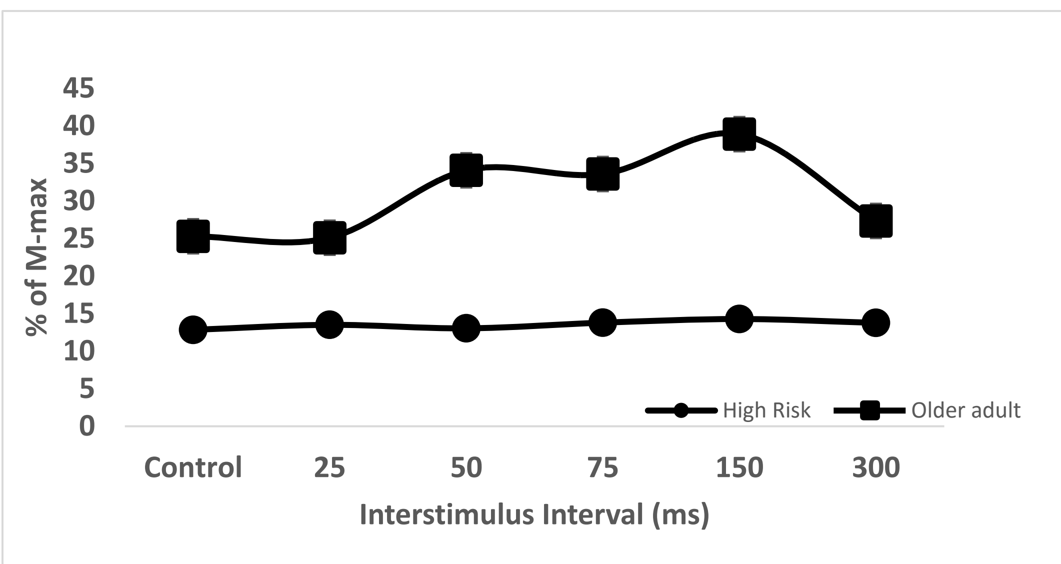

Figure 6: Results showed a significant interaction between older adult and high risk groups. Differences between groups are most prominent at longer-latency intervals (50ms, 75ms, and 150ms).

Chapter 5

Discussion of Results

Based on the results presented in this chapter, it can be concluded that contralateral common peroneal nerve conditioning results in modulation, specifically facilitation, of the soleus H-reflex in older adults, but not in high-risk fallers. Older adults demonstrate a facilitation at 50 ms, 75 ms, and 150 ms intervals. These results are similar to those obtained using a mechanical tendon-tap perturbation (Kamen & Koceja, 1989). Our findings are also consistent with those found by Ryder and colleagues (Ryder et al., *in review*).

While the older adult group exhibited significant changes in the H-reflex across different intervals, the high-risk-faller group showed no modulation across the same intervals. This suggests an inability to properly modulate spinal reflexes in this population, which could be a crucial element in successfully recovering from a perturbation. As a result, these individuals are at a higher risk of experiencing a fall and suffering from fall-related injuries. For example, the high-risk group demonstrated very little modulation across any of the tested intervals, suggesting an inability of information transfer from one limb to the other. In this group, the effect was similar for all intervals examined. Of course, one limitation of the current study was the small sample of high-risk fallers tested.

Future work should examine the time-course modulation of crossed-spinal reflexes in greater detail. Due to the fact that current literature has uncovered a very short latency (3ms – 30 ms) inhibition in healthy young individuals (Stubbs, Nielsen, Sinkjær, & Mrachacz-Kersting, 2011), the need to closely examine the modulation of this pathway over a more detailed time profile will be beneficial to developing a complete understanding of how this pathway is modulated and the potential mechanism responsible for this modulation (e.g. spinal mechanisms vs. descending tonic mechanisms).

Conclusions

The risk of falling among adults over the age of 65 is a very serious concern, as one third of this population experiences at least one fall annually (Tromp et al., 2001). These falls are the leading cause of both fatal and non-fatal injury in older adults, and resulted in over 19 billion dollars in medical expenses in 2000 (Stevens, Corso, Finkelstein, & Miller, 2006).

The purpose of this study was to compare crossed-spinal H-reflex modulation between healthy older adult subjects and older adults who are at a high risk of falling. The goal was to identify neural modulatory differences that could describe why a person falls, and possibly offer a predictor for individuals at risk of falling. Based on the results, older adults who experience frequent falls do not properly modulate spinal reflexes in response to perturbations. The ability to modulate could be a crucial component in recovering from external perturbations and preventing falls, so the inability to do so could provide insight as to why these individuals fall more frequently than neurologically healthy older adults.

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